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Multidrug Resistant Staphylococcus Aureus In Selected Health Care facilities in South Western Nigeria

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Abstract - Staphylococcus aureus is gradually becoming a problematic pathogen. It is associated with widespread drug resistance. In this study, multi-drug resistance among Staphylococcus aureus from clinical samples was investigated. Various clinical samples were collected from three hospitals selected for the study: Bowen University Teaching Hospital (BUTH), Ogbomoso Oyo State, Ladoke Akintola University of Technology (LAUTECH) University Health Centre, Ogbomoso Oyo State and University of Ilorin Teaching Hospital (UITH), Ilorin Kwara State. Staphylococcus aureus strains were isolated from the samples and tested for antibiotic susceptibility using disc method of media diffusion technique. Data obtained were subjected to statistical analysis. A total of 122 samples were collected, 17 (13.93%) from UITH, 61 (50%) from BUTH, and 44 (36.07%) from LAUTECH. Majority of the samples collected (56; 45.9%) were wound swabs. All the samples yielded Staphylococcus aureus. All the isolates were resistant to three or more of the antibiotics and they varied in their susceptibility to the other ten antibiotics. Multidrug resistant (MDR) Staphylococcal aureus were prevalent in the selected hospitals, but there was no significant difference in the prevalence of MDR Staphylococcus aureus in the hospitals. The significance of presence of MDR Staphylococcus aureus to antibiotic therapy and management of patients were discussed.

Keywords - Antibiotics, MDR, Staphylococcus aureus, Hospitals.

INTRODUCTION

Staphylococus aureus is frequently found as part of the normal flora on the skin and nasal passages. About 20% of the human population are long-term carriers of S. aureus [1,2]. Staphylococcus aureus can cause a range of illnesses; these include bacteraemia, endocarditis, meningitis and brain abscess, pneumonia, empyema, septic arthritis and osteomyelitis, abscesses of solid organs, pyomyositis, and soft tissue infections [3]. It is gradually gaining recognition as being resistant to antibiotics. Penicillin- resistant S. aureus, caused primarily by a S. aureus clone known as phage-type 80/81 was pandemic in the 1950s and early 1960s. However, the pandemic phage-type 80/81 S. aureus infections declined after the introduction of methicillin [4]. Some strains of S. aureus also exhibits resistance to antiseptics and disinfectants, which may aid their survival in hospital environment [5]. Methicillin resistance in Staphylococcus aureus is becoming widespread; and the term methicillin resistant Staphylococcus aureus (MRSA) is used to refer to the methicillin resistant strains. Resistance to methicillin is mediated via the mec operon, part of the staphylococcal cassette chromosome mec (SCCmec). Resistance is conferred by the mecA gene, which codes for an altered penicillin-binding protein (PBP2a or PBP2') that has a lower affinity for binding β-lactams (penicillins, cephalosporins, and carbapenems). Most methicillin-resistant strains are also multi-drug resistant [5,18] . Methicillin resistant S. aureus has since spread and is endemic in most hospitals worldwide. Community acquired MRSA (CAMRSA) was first reported in the 1990s and has emerged worldwide [6]. Uncontrolled antimicrobial use is likely to fuel the emergence of CAMRSA as well as drug resistance in a broad range of other human pathogens. Resistance, as a consequence of horizontal gene transfer, is initially encountered in hospitals and healthcare institutions where the selective pressures for resistance are greatest.

Skin and soft-tissue infections are the most common type of CA-MRSA infection, accounting for approximately 90% of cases, of which 90% are abscesses and/or cellulitis with purulent drainage. CA-MRSA strains also appear to be especially virulent with the capacity to cause fulminant, overwhelming infections, such as necrotizing fasciitis, necrotizing pneumonia, bone and joint infections accompanied by septic thromboembolic disease, purpura fulminans with or without Waterhouse-Friderichsen syndrome, orbital cellulitis and endophthalmitis, infections of the central nervous system, and bacteraemia and endocarditis [7]. The overall burden of staphylococcal diseases particularly those caused by methicillin resistant S. aureus (MRSA) strains is increasing in many countries; in both healthcare and community settings. CA-MRSA has had a profound impact on empirical therapy of suspected staphylococcal infection. Where CA-MRSA is prevalent antimicrobial therapy for treatment of staphylococcal infection, should be directed against MRSA. CA-MRSA strains are not merely escapees from healthcare facilities; their genotypes indicate that they are not closely related to endemic hospital clones and these community strains are susceptible to numerous antibiotics to which hospital

strains are routinely resistant. Two molecular markers not found in typical hospital MRSA are strongly associated with emergence of CA-MRSA regardless of geographical origin: a specific cassette element encoding mecA and genes encoding Panton-Valentine leukocidin (PVL) [8]. This study is to determine the prevalence of multi-drug resistance in Staphylococcus aureus isolates from three hospitals. Antibiotics susceptibility in Staphylococcus aureus isolates will be evaluated and the prevalence of multi-drug resistance profiled.

MATERIALS AND METHODS

Area of study

The study involved three hospitals: Bowen University Teaching Hospital (BUTH), Ogbomoso Oyo State, Ladoke Akintola University of Technology (LAUTECH) University Health Centre, Ogbomoso Oyo State and University of Ilorin Teaching Hospital (UITH), Ilorin Kwara State. Clinical samples consisting of wound swab, urine, blood, aspirate, ear swab, sputum, and high vaginal swab were collected from patients attending the Medical Microbiology Laboratory Department of the three hospitals between July 2010 and December 2011. Staphylococcus aureus strains were isolated from the samples using standard culture techniques [9]. The identity of the isolates were confirmed using biochemical characteristics.

Susceptibility Testing

Standardized pure cultures of the isolates were prepared and tested for susceptibility to various antibiotics the disc method of media diffusion technique. Commercial disc of the following antibiotics were used: Drovid (D- 10µg), cephalexin (CX- 20µg), norfloxacin (NB- 10µg), clindamycin (CD- 10µg), cotrimoxazole (COT- 25µg), amoxycillin (AX- 20µg), erythromycin (E- 10µg), gentamycin (G- 10µg), ciprofloxacin (CIP- 5µg), augmentin (AUG- 30µg), azithromycin (ATH- 15µg), ofloxacin (OFX- 30µg), cefriaxone (CRO- 30µg), cefuroxime (CXM- 30µg), zithromax (Z- 30µg), novobiocin (NV- 30µg), vancomycin (VA- 30µg), netilmicin (NET- 10µg), pentylenetetrazol (PTZ- 15µg), sulbactam (SAM- 20µg), and ceftazidime (CAZ- 30µg). The plates were incubated at 37°C for 24 hours. The diameter of zones of inhibition that developed was measured and interpreted as sensitive, intermediate sensitive, or resistance CLSI [9]

RESULTS

A total of 122 samples were collected, 17 (13.93%) of them were obtained from University of Ilorin Teaching Hospital (UITH), 61 (50%) were obtained from Bowen University Teaching Hospital (BUTH), and 44 (36.07%) were obtained from Ladoke Akintola University of Technology (LAUTECH) (Figure 1). Majority of the samples collected (56; 45.9%) were wound swabs, the fewest samples were leg ulcer and scrotal wound (2; 1.64% each). The frequency of the samples is shown on Figure 2. All the samples yielded strains of Staphylococcus aureus.

The antibiotic susceptibility patterns of the isolates are shown on Figure 3. All the isolates (100%) were resistant to ceftazidime, cotrimoxazole, and amoxycillin. There were varying extents of resistance to the other antibiotics: 113 of the isolates (92.62%) were resistant to cephalexin, 83 (68.03%) were resistance to azithromycin. Less than 50% of the isolates were resistant to the other antibiotics. None of the isolates was resistant to augmentin, drovid, zithromax, novobiocin, vancomycin, pentylenetetrazol, sulbactam, and netilmicin. All of the isolates from sputum and urine were found to be resistant to cephalexin, ceftazidime, cotrimoxazole, and amoxycillin. All the isolates from pus were resistant to norfloxacin. Similarly, all isolates from ear swab were resistant to clindamycin. All the isolates from leg ulcer were resistant to azithrmycin. The isolates showed no resistance to drovid from wound. Similarly, S. aureus showed no resistance to ciprofloxacin from aspirate. All the isolates from blood were found to be resistant to cephalexin, ceftazidime, cotrimoxazole, and amoxycillin. S. aureus was resistant to gentamycin from high vaginal swab. The occurrence of the resistant strains in the selected hospital is presented on Table 1. The highest case of resistance was against gentamycin by Strains from LAUTECH samples. Some of the isolates showed multi-drug resistant. Statistical analysis showed there was no significant difference in prevalence between the hospitals (Fisher statistical value (F) 0.68 against the significant value (P) of 0.78).

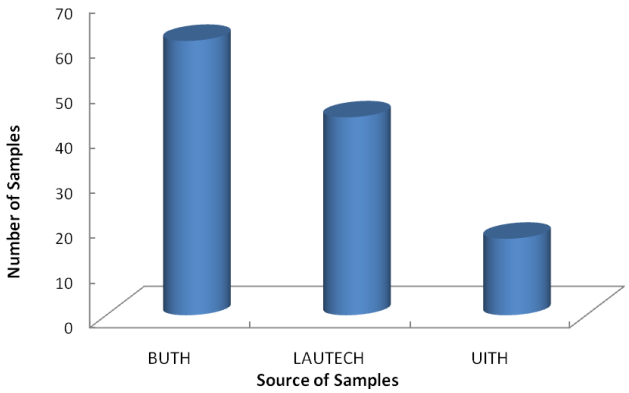

Figure 1. Distribution of Samples Positive for Staphylococcus aureus among Sources

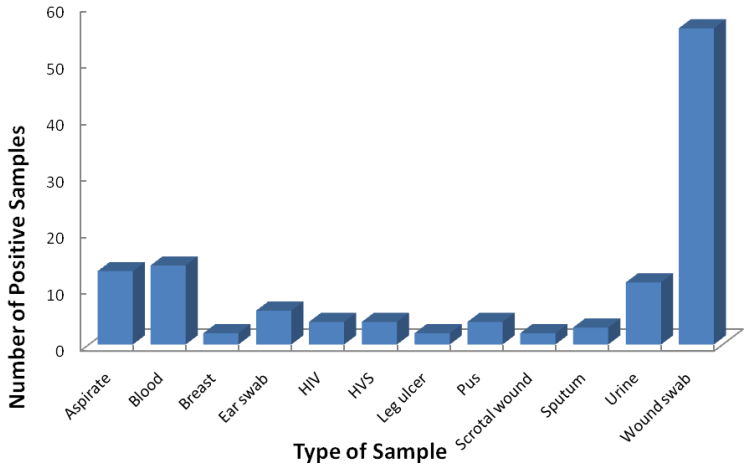

Figure 2: Samples positive for Staphylococcus aureus and their Frequencies

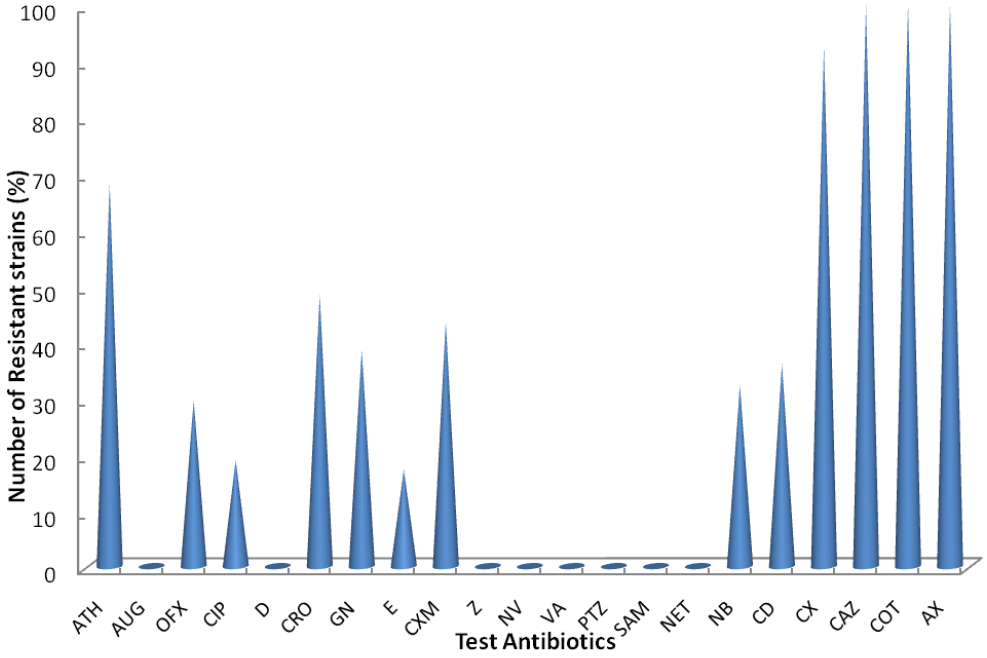

Figure 3. Antibiotic Susceptibility Pattern of *Staphylococcus aureus* from Clinical samples

Key:
D: Drovid CX: Cephalexin, NB: Norfloxacin CD: Clindamycin, CAZ: Ceftazidime
COT: Cotrimoxazole, AX: Amoxycillin, E: Erythromycin GN: Gentamycin
CIP: ciprofloxacin, AUG: Augmentin, ATH: Azithromycin, OFX: Ofloxacin CRO: cefriaxone, CXM: Cefuroxime, Z: Zithromax, NV: Novobiocin, VA: vancomycin, NET: Netilmicin, PTZ: pentylenetetrazol, SAM: sulbactam

Table 1. Incidence of Drug Resistant Staphylococcus aureus strains in Location

Antibiotics	Number of Resistant Strains (%)		
	UITH	BUTH	LAUTECH
Azithromycin	29.41	52.94	64.71
Ofloxacin	41.18	11.76	17.65
Ciprofloxacin	47.06	5.88	11.76
Cefriaxone	47.06	64.71	41.18
Gentamycin	41.18	29.41	70.59
Erythromycin	52.94	5.88	11.76
Cefuroxime	64.71	41.18	35.29
Norfloxacin	35.29	35.29	47.06
Clindamycin	64.71	23.53	52.94
Cephalexin	94.12	88.24	100.00
Ceftazidime	100.00	100.00	100.00
Cotrimoxazole	100.00	100.00	100.00
Amoxycillin	100.00	100.00	100.00

DISCUSSION

Prevalence of staphylococcus aureus has been a major nasal carriage problem in Nigeria and around the world [1], leading to various kind of infections in virtually every body parts. From this study, evidently the occurrence of Staphylococcus aureus in wounds samples is indicative of poor wound hygiene; allowing for contamination of the wounds. This suggests that the wounds are likely to have become dirty. Such wounds are likely to have microbial biofilms in place, which will make managing the wound more challenging. Also the study samples appears to be cases of bacteriuria and bacteraemia as evidenced from the recovery of Staphylococcus aureus from urine, blood and other clinical samples investigated as evidently seen in Fig 2. Establishment of Staphylococcus aureus in the blood is particularly a serious challenge considering the chances of dissemination the organisms to other part of the body and to organs through the blood.

From the study the Staphylococcus aureus isolates showed varying degree of resistance to the antibiotics tested, confirming the menace of resistance posed by this bacteria in public and community health sectors. [1, 2, 11]. Strains from wound infections were found to be particularly resistant to the drugs tested as confirmed by previous reports. All the strains isolated were resistant to ceftazidime, cotrimoxazole, and amoxicillin, this suggest an abuse or misuse of the drugs, which could have allowed for the emergence of resistant strains. The resistance pattern of the strains showed that most of the Staphylococcus aureus encountered were resistant to one or more drugs. This seems to confirm the observation that about 70 percent of the bacteria that cause infections in hospitals are resistant to at least one of the drugs most commonly used for treatment [10, ,11, 12, 18].

Resistance shown by the Staphylococcus aureus strains is in accordance with previous reports of demonstration of drug resistance by Staphylococcus aureus strains. Gentamicin-resistant strains were observed in this study as reported elsewhere [11, 12]. Likewise Ofloxacin-resistant strains were also reported [13]. Other previous work also reported ceftazidime-resistance among Staphylococcus aureus strains [14].

Comparing various locations in this study, resistance was predominantly observed in strains isolated from samples obtained at LAUTECH Teaching hospital. This suggests that there is a greater chance of non-compliance with therapy, and or misuse of drug in the areas surrounding the hospital. Although there were variations in the percentage of resistant strains encountered in each location, Statistical analysis showed there was no significant difference in the incidence of multidrug resistance between the locations. This is attributable to the facts that, attitude to patient management, drug use and administration are not substantially different in the three localities considered. Likewise over-the-counter antibiotics (penicillin [including cloxacillin], cephalosporins, tetracyclines, quinolones, and co-trimoxazole) are available. These drugs are frequently self-administered for inappropriate indications, and taken for irregular durations, hence encouraging the emerging of drug resistant strains [15, 18]. Evidently from above this could be the major reason for the level of resistance observed in this work, with each isolates showing one or three minimum resistance to antibiotics employed during the course of this research study.

In view of the spread of drug resistance among the Staphylococcus aureus strains observed, it may be necessary to embark on multidrug therapy or combined therapy in managing Staphylococcus aureus infection. The profile of drug resistance calls for a serious concern. It may be a pointer of looming danger. It has been suggested that unless antibiotic resistance problems are detected as they emerge, and actions are taken immediately to curtail them, society could be faced with previously treatable diseases that have become again untreatable, as in the days before antibiotics were developed [16]. Antimicrobial resistance, or the ability of microorganisms to withstand treatment with drugs to which they were once susceptible, is a significant and multifaceted public health problem, the burden is worsened by the emergence of multidrug resistant strains.

The solution might not necessarily be the development of new drug but a change in the approach to management of patients. Other workers indicated that nearly 50% of antimicrobial use in hospitals is unnecessary or inappropriate [5,17, 18]. There is no doubt that this overuse of antibiotics is contributing to the growing challenges posed by antibiotic-resistant bacteria in many hospitals. An approach that requires that patient are administered their drug under supervision to avoid the menace of the superbugs and this could go a long way in checking the problem of drug resistance. [17, 18].

REFERENCE

[1] Kluytmans J, van Belkum A, Verbrugh H. Nasal carriage of Staphylococcus aureus: epidemiology, underlying mechanisms, and associated risks. Clin Microbiol Rev. 1997;10:505–20.

[2] Tenover F. C. Characterization of Staphylococcus aureus isolates from nasal cultures collected from individuals in the United States in 2001 to 2004. J Clin Microbiol.2008; 46:2837–41.

[3] Shaw K. J.In vitro activity of TR-700, the antibacterial moiety of the prodrug TR-701, against linezolid-resistant strains. Antimicrob Agents Chemother.2008;52:4442–7.

[4] Lentino J. R, Narita M, Yu V. L. New antimicrobial agents as therapy for resistant gram-positive cocci. Eur J Clin Microbiol Infect Dis. 2008;27:3–15.

[5] Liu C. A population-based study of the incidence and molecular epidemiology of methicillin-resistant Staphylococcus aureus disease in San Francisco, 2004–2005.Clin Infect Dis. 2008;46:1637–46.

[6] Kuehnert M. J. Prevalence of Staphylococcus aureus nasal colonization in the United States, 2001–2002.J Infect Dis. 2006;193:172–9.

[7] Hope R, Livermore D. M, Brick G, Lillie M, Reynolds R. Non-susceptibility trends among staphylococci from bacteraemias in the UK and Ireland, 2001–06. J Antimicrob Chemother.2008;62(Suppl 2):ii65–74.

[8] Voyich J. M. Is Panton-Valentine leukocidin the major virulence determinant in community-associated methicillin-resistant Staphylococcus aureus disease? J Infect Dis. 2006;194:1761–70.

[9] National Committee for clinical laboratory standards (2005): Performance Standards for Antimicrobial Susceptibility test; Institute (CLSI) antimicrobial susceptibility testing standards: M2-A9 and M7-A7.

[10] Lodise T. P, Lomaestro B, Graves J, Drusano GL. Larger vancomycin doses (at least four grams per day) are associated with an increased incidence of nephrotoxicity. Antimicrob Agents Chemother.2008;52:1330–6.

[11] Pannaraj P. S, Hulten K. G, Gonzalez B. E, Mason E. O, Jr, Kaplan S. L. Infective pyomyositis and myositis in children in the era of community-acquired, methicillin-resistant Staphylococcus aureus infection. Clin Infect Dis. 2006;43:953–60.

[12] Stam-Bolink E. M, Mithoe D, Baas W. H, Arends J. P, Moller A. V. Spread of a methicillin-resistant Staphylococcus aureus ST80 strain in the community of the northern Netherlands. Eur J Clin Microbiol Infect Dis. 2007;26:723–7.

[13] Shinefield H. Use of a Staphylococcus aureus conjugate vaccine in patients receiving hemodialysis.N Engl J Med. 2002;346:491–6.

[14] Mato R. Clonal types and multidrug resistance patterns of methicillin-resistant Staphylococcus aureus (MRSA) recovered in Italy during the 1990s. Microb Drug Resist. 2004;10:106–13.

[15] Shorr A. F, Kunkel M. J, Kollef M. Linezolid versus vancomycin for Staphylococcus aureus bacteraemia: pooled analysis of randomized studies. J Antimicrob Chemother.2005;56:923–9.

[16] Gillet Y. Factors predicting mortality in necrotizing community-acquired pneumonia caused by Staphylococcus aureus containing Panton-Valentine leukocidin.Clin Infect Dis. 2007;45:315–21.

[17] Burlak C. Global analysis of community-associated methicillin-resistant Staphylococcus aureus exoproteins reveals molecules produced in vitro and during infection. Cell Microbiol.2007;9:1172–90.

[18] Olowe OA, Kukoyi OO, Taiwo SS, Ojurongbe O, Opaleye OO, Bolaji OS, Adegoke AA, Makanjuola OB, Ogbolu DO, Alli OT Phenotypic and molecular characteristics of methicillin-resistant Staphylococcus aureus isolates from Ekiti State, Nigeria Infection and Drug Resistance 2013, 6:87-9